09/ 574,740

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NEWS	4	Jul 15	Data from 1960-1976 added to RDISCLOSURE
NEWS	5	Jul 21	Identification of STN records implemented
NEWS	6	Jul 21	Polymer class term count added to REGISTRY
NEWS	7	Jul 22	INPADOC: Basic index (/BI) enhanced; Simultaneous Left and Right Truncation available
NEWS	8	AUG 05	New pricing for EUROPATFULL and PCTFULL effective August 1, 2003
NEWS	9	AUG 13	Field Availability (/FA) field enhanced in BEILSTEIN
NEWS	10	AUG 15	PATDPAFULL: one FREE connect hour, per account, in September 2003
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NEWS	14	AUG 18	Data available for download as a PDF in RDISCLOSURE
NEWS	15	AUG 18	Simultaneous left and right truncation added to PASCAL
NEWS	16	AUG 18	FROSTI and KOSMET enhanced with Simultaneous Left and Righ Truncation
NEWS	17	AUG 18	Simultaneous left and right truncation added to ANABSTR
NEWS	18	SEP 22	DIPPR file reloaded
NEWS	19	SEP 25	INPADOC: Legal Status data to be reloaded
NEWS	20	SEP 29	DISSABS now available on STN

NEWS EXPRESS	OCTOBER 01 CURRENT WINDOWS VERSION IS V6.01a, CURRENT MACINTOSH VERSION IS V6.0b(ENG) AND V6.0Jb(JP), AND CURRENT DISCOVER FILE IS DATED 23 SEPTEMBER 2003
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NEWS PHONE	Direct Dial and Telecommunication Network Access to STN
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* * * * * * * * * * * * * * STN Columbus * * * * * * * * * * * * * * *

FILE 'HOME' ENTERED AT 10:08:23 ON 10 OCT 2003

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COST IN U.S. DOLLARS                                    SINCE FILE      TOTAL
                                                           ENTRY    SESSION
FULL ESTIMATED COST                                         0.21       0.21

FILE 'REGISTRY' ENTERED AT 10:08:33 ON 10 OCT 2003
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STRUCTURE FILE UPDATES:     8 OCT 2003  HIGHEST RN 601453-92-3
DICTIONARY FILE UPDATES:    8 OCT 2003  HIGHEST RN 601453-92-3

TSCA INFORMATION NOW CURRENT THROUGH JULY 14, 2003

  Please note that search-term pricing does apply when
  conducting SmartSELECT searches.

Crossover limits have been increased.  See HELP CROSSOVER for details.

Experimental and calculated property data are now available.  See HELP
PROPERTIES for more information.  See STNote 27, Searching Properties
in the CAS Registry File, for complete details:
http://www.cas.org/ONLINE/STN/STNOTES/stnotes27.pdf

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COST IN U.S. DOLLARS                                    SINCE FILE      TOTAL
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FULL ESTIMATED COST                                         0.80       1.01

FILE 'REGISTRY' ENTERED AT 10:09:31 ON 10 OCT 2003
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Property values tagged with IC are from the ZIC/VINITI data file
provided by InfoChem.

STRUCTURE FILE UPDATES:     8 OCT 2003  HIGHEST RN 601453-92-3
DICTIONARY FILE UPDATES:    8 OCT 2003  HIGHEST RN 601453-92-3

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Experimental and calculated property data are now available.  See HELP
PROPERTIES for more information.  See STNote 27, Searching Properties
in the CAS Registry File, for complete details:
http://www.cas.org/ONLINE/STN/STNOTES/stnotes27.pdf

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L1      STRUCTURE UPLOADED

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09/ 574,740

L1 HAS NO ANSWERS
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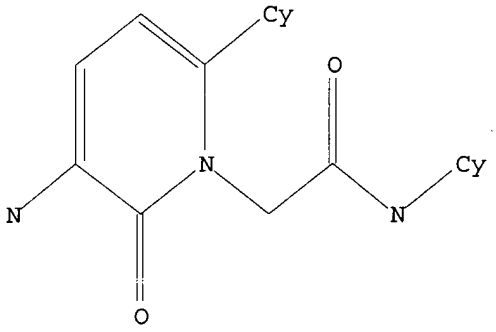

Structure attributes must be viewed using STN Express query preparation.

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FULL SCREEN SEARCH COMPLETED - 4570 TO ITERATE

100.0% PROCESSED 4570 ITERATIONS 3 ANSWERS
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L2 3 SEA SSS FUL L1

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COST IN U.S. DOLLARS SINCE FILE ENTRY TOTAL SESSION
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FILE COVERS 1907 - 10 Oct 2003 VOL 139 ISS 16
FILE LAST UPDATED: 9 Oct 2003 (20031009/ED)

This file contains CAS Registry Numbers for easy and accurate substance identification.

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L3 3 L2

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YOU HAVE REQUESTED DATA FROM 3 ANSWERS - CONTINUE? Y/(N):y

L3 ANSWER 1 OF 3 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1998:788773 CAPLUS
DOCUMENT NUMBER: 130:66805
TITLE: Preparation of peptide inhibitors of interleukin-1.beta. converting enzyme
INVENTOR(S): Bemis, Guy W.; Golec, Julian M. C.; Lauffer, David J.; Mullican, Michael D.; Murcko, Mark A.; Livingston, David J.
PATENT ASSIGNEE(S): Vertex Pharmaceuticals, Incorporated, USA
SOURCE: U.S., 106 pp., Cont.-in-part of U.S. 5,656,627.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 3
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 5847135	A	19981208	US 1995-440898	19950525
US 5756466	A	19980526	US 1994-261452	19940617
US 5656627	A	19970812	US 1995-405581	19950317
US 5716929	A	19980210	US 1995-464964	19950605
US 6103711	A	20000815	US 1995-465216	19950605
TW 509698	B	20021111	TW 1995-84105903	19950609
IN 181338	A	19980516	IN 1995-CA659	19950612
CA 2192089	AA	19951228	CA 1995-2192089	19950616
WO 9535308	A1	19951228	WO 1995-US7617	19950616
W: AM, AT, AU, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LT, LU, LV, MD, MG, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TM, TT				
RW: KE, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
AU 9529446	A1	19960115	AU 1995-29446	19950616
AU 709114	B2	19990819		
EP 784628	A1	19970723	EP 1995-925257	19950616
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BR 9508051	A	19971021	BR 1995-8051	19950616
HU 76622	A2	19971028	HU 1996-3475	19950616
JP 10504285	T2	19980428	JP 1996-502478	19950616
AP 797	A	20000107	AP 1997-960	19950616
W: KE, MW, SD, SZ, UG				
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FI 9605036	A	19970214	FI 1996-5036	19961216
BG 63634	B1	20020731	BG 1997-101130	19970114
US 5973111	A	19991026	US 1997-828941	19970328
IN 183119	A	19990911	IN 1997-CA778	19970430
US 6420522	B1	20020716	US 1999-430822	19991029
US 2002099042	A1	20020725	US 2001-886773	20010621

PRIORITY APPLN. INFO.:

US 1994-261452	A2	19940617
US 1995-405581	A2	19950317
US 1995-440898	A3	19950525
US 1995-465216	A3	19950605
IN 1995-CA659	A1	19950612
WO 1995-US7617	W	19950616
US 1999-430822	A3	19991029

OTHER SOURCE(S): MARPAT 130:66805
AB Interleukin-1.beta. converting enzyme inhibitors R1NHX1[(CH2)mT](CH2)gR3 (X1 = CH, N; g = 0, 1; m = 0-2; T = a cyclic group, OH, CF3, COCO2H, CO2H; R1 = R4ZNR5CR6R7CO or substituted derivs., where R4 represents certain ring systems; R5 = H, a cyclic group, alkyl, arylcarbonyl, arylsulfonyl,

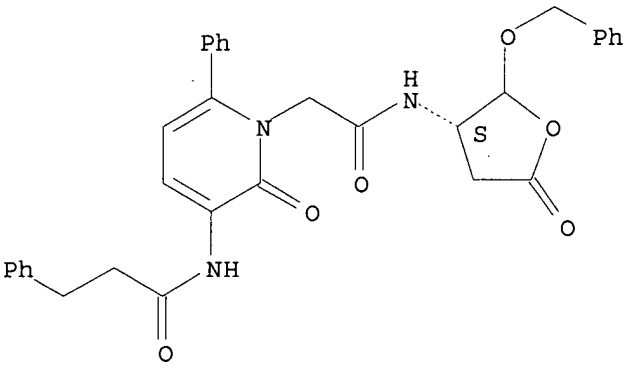
etc.; CR6R7 form a satd. carbocyclic or heterocyclic ring; R3 = CN, 1-alkenyl, alkoxyiminomethyl) were prepd. Thus, N-(N-acetyltyrosinylvalinylpipecolyl)-3-amino-4-oxobutanoic acid was prepd. and showed IC50 = 6-11 .mu.M for inhibition of interleukin-1.beta. converting enzyme.

IT **195071-94-4P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn. of peptide inhibitors of interleukin-1.beta. converting enzyme)

RN 195071-94-4 CAPLUS

CN 1(2H)-Pyridineacetamide, 2-oxo-3-[(1-oxo-3-phenylpropyl)amino]-6-phenyl-N-[(3S)-tetrahydro-5-oxo-2-(phenylmethoxy)-3-furanyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 50 THERE ARE 50 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 2 OF 3 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1997:541852 CAPLUS
DOCUMENT NUMBER: 127:234612
TITLE: Preparation of heterocyclyl aspartaldehyde peptide derivatives as interleukin-1.beta. converting enzyme inhibitors
INVENTOR(S): Bemis, Guy W.; Golec, Julian M. C.; Lauffer, David J.; Mullican, Michael D.; Murcko, Mark A.; Livingston, David J.
PATENT ASSIGNEE(S): Vertex Pharmaceuticals, Inc., USA
SOURCE: U.S., 67 pp., Cont.-in-part of U.S. Ser. No. 261,452. CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 3
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 5656627	A	19970812	US 1995-405581	19950317
US 5756466	A	19980526	US 1994-261452	19940617
US 5847135	A	19981208	US 1995-440898	19950525
US 5716929	A	19980210	US 1995-464964	19950605
US 6025147	A	20000215	US 1995-460973	19950605
TW 509698	B	20021111	TW 1995-84105903	19950609
IN 181338	A	19980516	IN 1995-CA659	19950612
ZA 9504988	A	19961217	ZA 1995-4988	19950615
CA 2192089	AA	19951228	CA 1995-2192089	19950616
WO 9535308	A1	19951228	WO 1995-US7617	19950616

W: AM, AT, AU, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LT, LU, LV, MD, MG, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TM, TT
RW: KE, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG

AU 9529446	A1	19960115	AU 1995-29446	19950616
AU 709114	B2	19990819		
EP 784628	A1	19970723	EP 1995-925257	19950616
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CN 1159196	A	19970910	CN 1995-194381	19950616
BR 9508051	A	19971021	BR 1995-8051	19950616
HU 76622	A2	19971028	HU 1996-3475	19950616
JP 10504285	T2	19980428	JP 1996-502478	19950616
AP 797	A	20000107	AP 1997-960	19950616
W: KE, MW, SD, SZ, UG				
NO 9605365	A	19970217	NO 1996-5365	19961213
FI 9605036	A	19970214	FI 1996-5036	19961216
BG 63634	B1	20020731	BG 1997-101130	19970114
US 5973111	A	19991026	US 1997-828941	19970328
IN 183119	A	19990911	IN 1997-CA778	19970430
US 6420522	B1	20020716	US 1999-430822	19991029
US 2002099042	A1	20020725	US 2001-886773	20010621

PRIORITY APPLN. INFO.:
US 1994-261452 A2 19940617
US 1995-405581 A2 19950317
US 1995-440898 A3 19950525
US 1995-465216 A3 19950605
IN 1995-CA659 A1 19950612
WO 1995-US7617 W 19950616
US 1999-430822 A3 19991029

OTHER SOURCE(S): MARPAT 127:234612

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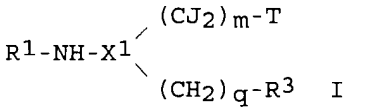

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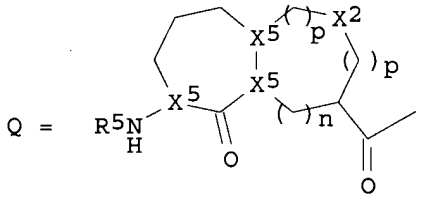

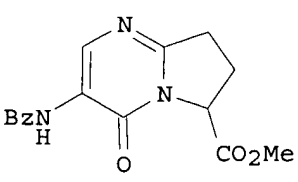

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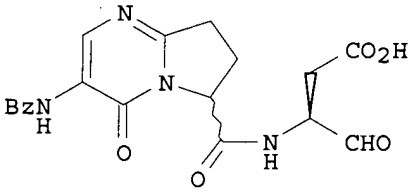


III

AB The present invention relates to novel classes of compds. I [X1 = CH, N; q = 0, 1; J = independently H, OH, F; m = 0-2; T = Ar3, OH, CF3, COCO2H, CO2H, COCH2OH, CONHOH, SO2NHR, SO3H, P(O)(OH)NH2, CONHCN, OSO3H, CONHSO2R16, PO3H2, P(O)(OH)OR16, P(O)(OH)R16, OPO3H2, OP(O)(OH)OR16,

OP(O)(OH)R16, NHPO3H2, NHP(O)(OH)OR16, NHP(O)(OH)R16, COCH:C(OH)CO2H, 5- or 6-membered heterocyclic ring; R16 = C1-6 alkyl; R1 = optionally substituted fragment Q; X2 = O, CH2, NH, S, S(O), SO2; X5 = CH, N; n = 0-1, d = 0-2, such that n + d + d = 2; R3 = CN, CH:CHR9, CH:NOR9, (CH2)1-3T1R9, CJ2R9, COR13, COCONR5R10; each R4 = H, Ar1, R9, T1R9, (CH2)1-3T1R9; each T1 = CH:CH, O, S, S(O), SO2, NR10, NR10CO, CO, O2C, CO2, CONR10, O2CNR10, NR10CONR10, SO2NR10, NR10SO2, NR10SO2NR10; R5 = H, Ar1, COAr1, SO2Ar1, R9, CONR9, CO2R9, SO2R9, CONAr1R10, SO2NAr1R10, CONR9R10, SO2NR9R10; R5 = Ar1, SO2Ar1, COR9, CONAr1R10, SO2NAr1R10, CONR9R10, SO2NR9R10; R9 = optionally substituted, straight or branched C1-6 alkyl; R10 = H, C1-6 straight or branched alkyl; R13 = H, Ar1, Ar2, R9, T1R9, (CH2)1-3T1R9; Ar1 = aryl, cycloalkyl, or heterocyclyl group contg. 1-3 rings and 3-15 ring atoms; Ar2 = optionally benzo-fused 5-membered heterocyclyl; Ar3 = optionally substituted Ph or 5-membered heterocyclic ring] which are inhibitors of interleukin-1.beta. converting enzyme. The ICE inhibitors of this invention are characterized by specific structural and physicochem. features. This invention also relates to pharmaceutical compns. comprising these compds. The compds. and pharmaceutical compns. of this invention are particularly well suited for inhibiting ICE activity and consequently, may be advantageously used as agents against interleukin-1 mediated diseases, including inflammatory diseases, autoimmune diseases and neurodegenerative diseases. This invention also relates to methods for inhibiting ICE activity and methods for treating interleukin-1 mediated diseases using the compds. and compns. of this invention. Thus, cyclocondensation of Et 2-aminopyrrolidine-5-carboxylate with 4-ethoxymethylene-2-phenyl-2-oxazolidin-2-one gave 32% pyrrolopyrimidine II. Sapon. of II, followed by coupling with tert-Bu (3S)-amino-4-oxobutanoate semicarbazone, diastereomer sepn., and deprotection, gave ICE inhibitors III. III and related compds. inhibited ICE with Ki = 0.011 to 35 .mu.M in a UV-visible assay and IC50 = 0.50 to >35 .mu.M in a cell assay.

IT **195071-94-4P**

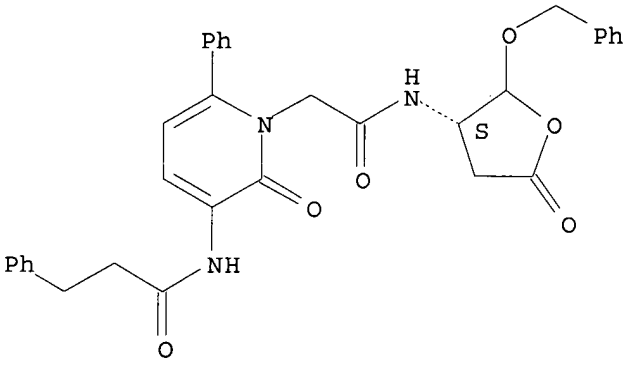
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(prepn. of heterocyclyl aspartaldehyde peptide derivs. as interleukin-1.beta. converting enzyme inhibitors)

RN 195071-94-4 CAPLUS

CN 1(2H)-Pyridineacetamide, 2-oxo-3-[(1-oxo-3-phenylpropyl)amino]-6-phenyl-N-[(3S)-tetrahydro-5-oxo-2-(phenylmethoxy)-3-furanyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L3 ANSWER 3 OF 3 CAPLUS COPYRIGHT 2003 ACS on STN

ACCESSION NUMBER: 1996:214750 CAPLUS

DOCUMENT NUMBER: 124:290273

TITLE: Preparation of peptide analogs as inhibitors of

09/ 574,740

interleukin-1 beta converting enzyme (ICE)

INVENTOR(S): Bemis, Guy W.; Golec, Julian M. C.; Lauffer, David J.; Mullican, Michael D.; Murcko, Mark A.; Livingston, David J.

PATENT ASSIGNEE(S): Vertex Pharmaceuticals Incorp., USA

SOURCE: PCT Int. Appl., 374 pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 3

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9535308	A1	19951228	WO 1995-US7617	19950616
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US 5656627	A	19970812	US 1995-405581	19950317
US 5847135	A	19981208	US 1995-440898	19950525
AU 9529446	A1	19960115	AU 1995-29446	19950616
AU 709114	B2	19990819		
EP 784628	A1	19970723	EP 1995-925257	19950616
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BR 9508051	A	19971021	BR 1995-8051	19950616
JP 10504285	T2	19980428	JP 1996-502478	19950616
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US 6420522	B1	20020716	US 1999-430822	19991029

PRIORITY APPLN. INFO.:

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OTHER SOURCE(S): MARPAT 124:290273

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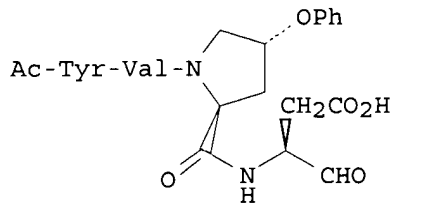

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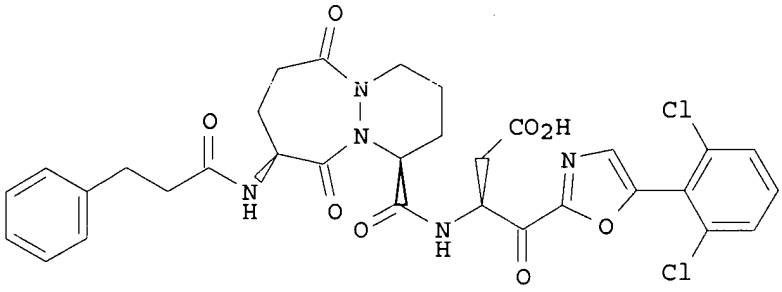


II

AB Novel classes of compds. are prepd., which are characterized by specific structural and physicochem. features comprising (a) a first and a second hydrogen bonding moiety, each of said moieties being capable of forming a hydrogen bond with a different backbone atom of ICE selected from the carbonyl O and the amide NH group of Arg-341 Ser-339, (b) a first and a second moderately hydrophobic moiety, said moieties each being capable of assocg. with a sep. binding pocket of ICE when the inhibitor is bound thereto, said binding pocket being selected form the P2, P3, P4, and P' binding pockets, and (c) an electroneg. moiety comprising .gtoreq.1 electroneg. atoms, said atoms being attached to the same atom or to adjacent atoms in the moiety and said moiety being capable of forming .gtoreq.1 hydrogen bonds or salts bridges with residues in the P1 binding pocket of ICE. These compds. and pharmaceutical compns. of this invention are particularly well suited for inhibiting ICE activity and consequently may be advantageously used as agents against interleukin-1 mediated diseases, including inflammatory diseases, autoimmune diseases and neurodegenerative diseases. Thus, etherification of Me N-tert-butoxycarbonyl-cis-4-hydroxyprolinate with phenol using Ph3P and di-Et azodicarboxylate in THF to Me N-tert-butoxycarbonyl-cis-4-phenoxyprolinate followed by deprotection with HCl in EtOAc to Me 4-phenoxyprolinate hydrochloride and condensation with Ac-Tyr-Val-OH using 1-ethyl-3-(3-dimethylaminopropyl)carbodiimide hydrochloride, HOBT, and diisopropylethylamine in DMF gave Me N-acetyl-L-tyrosinyl-L-valyl-(4-phenoxy)prolinate. Sapon. of the latter peptide ester with LiOH in aq. THF to N-acetyl-L-tyrosinyl-L-valyl-(phenoxy)proline followed by condensation with N-allyloxycarbonyl-4-amino-5-benzyloxy-2-oxotetrahydrofuran gave N-[N-acetyl-L-tyrosinyl-L-valyl-(4-phenoxy)prolinyl]-4-amino-5-benzyloxy-2-oxotetrahydrofuran (1:1 diastereomer mixt.), which underwent hydrogenolysis over Pd(OH)2 in MeOH under H atm. to give the title compd. (I). In a IL-1.beta. assay with a mixed population of human peripheral blood mononuclear cells or enriched adherent mononuclear cells, I in vitro showed IC50 of 2.6 and 0.25 .mu.M for inhibiting the processing of pre-IL-1.beta. by ICE.

IT **175210-99-8P 175415-31-3P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn. of peptide analogs as inhibitors of interleukin-1 beta converting enzyme for treating inflammatory, autoimmune and neurodegenerative diseases)

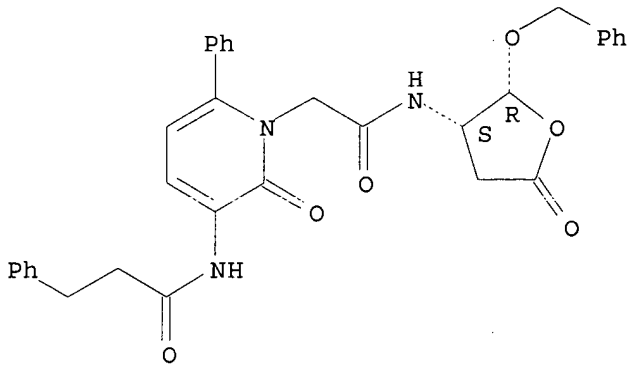
RN 175210-99-8 CAPLUS

CN 1(2H)-Pyridineacetamide, 2-oxo-3-[(1-oxo-3-phenylpropyl)amino]-6-phenyl-N-

09/ 574,740

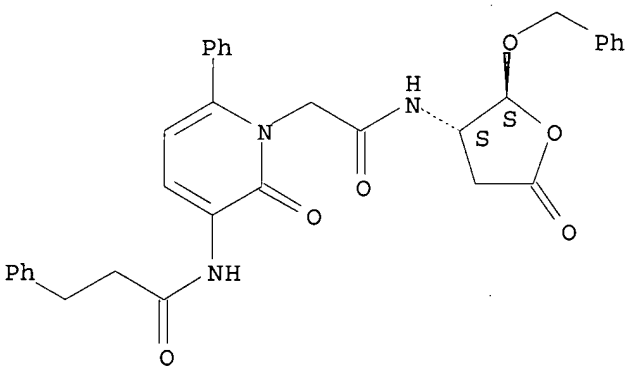
[tetrahydro-5-oxo-2-(phenylmethoxy)-3-furanyl]-, (2R-cis)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 175415-31-3 CAPLUS
CN 1(2H)-Pyridineacetamide, 2-oxo-3-[(1-oxo-3-phenylpropyl)amino]-6-phenyl-N-[tetrahydro-5-oxo-2-(phenylmethoxy)-3-furanyl]-, (2S-trans)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



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L3 3 S L2

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COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	14.03	163.19

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)	SINCE FILE	TOTAL

09/ 574,740

	ENTRY	SESSION
CA SUBSCRIBER PRICE	-1.95	-1.95

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